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Oncological Outcome after Laparoscopic Radical Prostatectomy: 10 years Experience

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Abstract

Objective—We analyzed the oncological outcome after laparoscopic radical prostatectomy (LRP) in a consecutive series of patients with prostate cancer.

Material and Methods—from 1998 to 2007, 1564 consecutive patients (median age 61 years, IQ range 56, 66) with clinically localized prostate cancer (cT1c–cT3a) were treated with LRP by two surgeons either at IMM (Paris, France) or MSKCC (New York, USA). Progression of disease was defined as a PSA of 0.1 ng/ml or greater with confirmatory rise, or initiation of secondary therapy and the information was available for 1422 patients. Patients were stratified as low, intermediate or high risk based on the pretreatment prostate cancer nomogram progression free probability of >90%, 89% to 71% and < 70% respectively.

Results—The overall 5-year and 8-year probability of freedom from progression was 78% (95% CI 74%–82%) and 71% (95% CI 63%, 78%) respectively. For low, intermediate and high risk cancer, the 5-year progression free probability was 91% (95% CI 85%–95%), 77% (95% CI 71%–82%) and 53% (95% CI 40%–65%) respectively. Surgical margins were positive in 13% of cases. The 5-year progression free probability was 49% (95% C.I. 35%–61%) when the surgical margins were positive vs. 83% (95% C.I. 79%–86%) in negative surgical margins cases. Nodal metastases were detected in 3% of the patients after limited pelvic lymph node dissection and in 10% after a standard pelvic lymph node dissection ($p < 0.001$). The 3 year probability of freedom from progression for node positive patients was 49%. There were 22 overall deaths and 2 deaths from prostate cancer.

Conclusion—Laparoscopic radical prostatectomy provided 5 and 8-year cancer control in 78 and 71% of patients with clinically localized prostate cancer and 53% of those with high risk cancers at 5 years. A pelvic lymph node dissection limited to the external iliac nodal group is inadequate for detecting nodal metastases.

Keywords

prostate neoplasm; laparoscopy; surgery

INTRODUCTION

Over the last century urology has seen major contributions in the surgical treatment of prostate diseases. In 1905, Hugh Hampton Young reported his technique and results of perineal

prostatectomy for prostate cancer¹. In 1948 Millin popularized the retropubic approach, which allowed via a wider surgical field the possibility of pelvic lymph node dissection and better knowledge of the intricate pelvic anatomy². In 1982 Walsh and Donker introduced the anatomical technique of nerve sparing radical prostatectomy, offering for the first time men with prostate cancer the possibility of sexual function preservation and thus, opening a new era in the surgical treatment of prostate cancer³. A number of technical modifications ensued which rendered open retropubic radical prostatectomy the standard treatment that provides men with clinically localized prostate cancer with the best chances for optimal outcome⁴.

In 1998, a standardized and reproducible technique of minimally invasive laparoscopic radical prostatectomy⁵ was published, which has shown promising short-term oncological outcome over the last decade^{6–8}. This approach achieved comparable positive surgical margin rates and quality of pelvic lymphadenectomy when prospectively compared to the open approach⁹ and has since gained worldwide acceptance.

Long-term oncological outcomes however, have been lacking. Herein, we report a detailed analysis of oncological outcome based on 10 years of consecutive experience of laparoscopic radical prostatectomy.

MATERIAL AND METHODS

Study population

From January of 1998 to July of 2007, 1564 consecutive patients (median age 61 years, IQ range 56, 66) with clinically localized prostate cancer (cT1c-cT3a) were treated with LRP at l'Institut Mutualiste Montsouris (Paris, France) or Memorial Sloan-Kettering Cancer Center (New York, USA) by one of two surgeons (BG and KT).

Study Design

This is an institutional review board approved retrospective analysis of prospectively collected data.

Preoperative treatment planning—Both surgeons used a uniform preoperative evaluation and risk assessment. Preoperative clinical parameters including patients' age, 2002 TNM clinical stage, preoperative prostate specific antigen (PSA), Gleason sum on prostate biopsies were prospectively recorded. Results from clinical staging, PSA level, Gleason sum, biopsy data, endorectal coil MRI findings and the patient's preoperative potency status along with Kattan's nomogram predicted disease risk¹⁰ were taken into consideration in the surgical planning since November 2002.

Surgical technique—This series includes the very first patients treated by LRP and therefore includes the period of trials and tribulation with the surgical technique, then the established Montsouris technique as described by Guillonnet and Vallencien¹¹. After June of 2003, modifications of the previously described Montsouris technique were introduced. One modification involved the apical dissection, with transection of the urethra at the end of the prostatectomy once the neuro-vascular bundles have been dissected off the apex and completely freed in order to delineate better the prostate apical anatomy. Furthermore, intra-operative gross examination of the specimen before completion of the urethrovesical anastomosis was systematically done¹².

Indications and anatomical limits of Pelvic lymph node dissection (PLND), between January of 1998 and January of 2005, the nomogram predicted probability of pelvic lymph node invasion was used to decide on the indication for PLND¹³. In general, patients with a predicted

lymph node invasion < 1% did not undergo a node dissection, whereas those with a probability > 1% underwent a PLND limited to the external iliac nodal group. This strategy was changed on February 1st, 2005, whereby all patients regardless of their risk stratification underwent a standard PLND including the external iliac, internal iliac and obturator fossa nodal groups.

Pathological examination—The radical prostatectomy specimen was coated with India ink to delineate the surgical margins then fixed in 10% formalin. Prostate and seminal vesicles were step sectioned transversely at 3–4 mm intervals. The prostate's most apical tissue was sectioned in the sagittal plane. Specimens were examined for the following variables: Gleason sum, pathological stage, seminal vesicle invasion, bladder neck invasion and extra prostatic extension. A positive surgical margin (PSM) was defined as presence of cancer at the inked margin of resection in the radical prostatectomy specimen, regardless of whether additional tissue was resected or not.

Postoperative Follow-up—Postoperatively, the planned PSA monitoring schedule consisted of a measurement at 6 weeks then every 6 months for 4 years, and then yearly afterwards. Progression of disease was defined as a PSA of 0.1 ng/ml or greater with confirmatory rise, or initiation of secondary therapy; this information was available for 1422 patients (91%).

Patients were stratified as low, intermediate or high risk based on the pretreatment prostate cancer nomogram progression free probability of >90%, 89% to 71% and < 70% respectively.

Statistical Analysis

The probability of freedom from recurrence following radical prostatectomy was estimated using Kaplan-Meier methods. Fisher's exact test was used to compare rates of lymph node involvement between patients with a standard or limited pelvic lymph node dissection. Only patients with a predicted probability of lymph node involvement >1% were compared, as this was the requirement for lymph node dissection before February 2005. All statistical analyses were conducted using Stata 10.0 (StataCorp LP, College Station, TX).

RESULTS

Clinical and pathological characteristics

The clinical and pathological features in this series fit the characteristics of prostate cancer treated in the modern post-PSA era. The intermediate and high risk groups as defined in this study represented 52% and 12% of the patient population respectively (Table 1). The overall positive surgical margin rate was 13%.

Oncological outcome

Survival and Progression—Only 2 patients died of prostate cancer during the study period, and 20 died of other causes. There was 1 local recurrence documented by biopsy and 10 cases of metastasis following surgery. Among the 1422 patients in our cohort, 153 experienced biochemical recurrence following surgery. The median follow up for patients without recurrence was 1.5 years; 167 patients (12%) were at recurrence-free at 5 years and followed for more than 5 years. The actuarial probability of remaining free of progression at 5 and 8 years postoperatively was 78% (95% CI 74%, 82%) and 71% (95% CI 63%, 78%) respectively (Figure 1). The 5-year progression free probability for men with low, intermediate and high risk prostate cancers was 91% (95% CI 85%–95%), 77% (95% CI 71%–82%) and 53% (95% CI 40%–65%) respectively (Figure 2). The freedom from progression at 5 years was 83% (95% CI 79%–86%) in patients with negative surgical margins and 49% (95% CI 35%–61%) in those with a positive surgical margin (Figure 3). When stratified by pathological stage, 5 year

freedom from progression of disease after laparoscopic radical prostatectomy was 83% (95% CI, 66%–91%) and 69% (95% CI, 52%–80%) for organ confined (pT2, node negative) and non-organ confined cancers (pT3, node negative) respectively (Figure 4).

Pelvic lymph node dissection—Among patients with a nomogram predicted probability of lymph node involvement greater than 1% and who had a lymph node dissection performed, the number of lymph nodes retrieved and positivity rate detected was higher among those treated by a standard PLND (internal iliac, external iliac and obturator fossa groups) vs. those treated by a limited PLND (external iliac group only) (3% vs. 10%, $p<0.001$) (Table 2). While no patient with positive lymph nodes was followed without recurrence to 5 years, the 3-year probability of freedom from recurrence for these patients was 49% (95% C.I. 32%, 64%) (Figure 4).

DISCUSSION

The introduction of the laparoscopic approach to perform radical prostatectomy was carried by the hope that better visualization and access to the tight confines of the male human pelvis would eventually translate into better oncological, functional and morbidity outcomes, and while hypothetically it all made sense, the available scientific evidence has not been able to confirm any major advantages. In fact the gold standard of evidence based medicine (ie: randomized study) has not been possible to duly accomplish in order to test the above hypothesis. Prospective comparative analysis of open and laparoscopic radical prostatectomy however, demonstrated equivalency of oncological results with regards to positive surgical margin rate, quality of pelvic lymph node dissection and short-term progression free probability⁹. One important clarification is that the endpoint of the present report is not a comparison of oncological efficacy of LRP vs. other approaches or treatment modalities but a description of oncological results of a 10 years experience with laparoscopic radical prostatectomy across all risk groups, the reported data in the literature is discussed in this manuscript to provide a perspective, and should by no means be used for a comparative analysis, since the methodology, timeframe of the study and endpoint definitions vary greatly from one study to another.

Large single institution experiences from either Europe or United States have reported favorable short-term oncological outcomes providing another level of evidence that cancer control after laparoscopic radical prostatectomy would compare favorably to other large series of open radical prostatectomy but long-term data is awaited^{6–8}. After a decade of laparoscopic radical prostatectomy, mid-term cancer control data is now available and shows that laparoscopic radical prostatectomy effectively controlled the disease in 79% and 77% of men with prostate cancer at 5 and 8 years respectively. Comparable results were reported by our MSKCC group using the open surgical approach, with 82%, 77% and 75% freedom from progression respectively at 5, 10 and 15 years after surgery¹⁴. We expect the overall mid-term oncological results obtained in this laparoscopic experience to continue to compare favorably with long-term results established with the open approach. However, evaluation of the overall results in a disease known for its heterogeneity and width of its prognostic significance spectrum with cancers ranging from totally indolent to rapidly lethal is not helpful for a given individual whose cancer carries particular features. Reporting of results based on risk groups can be more informative. When stratified by risk of disease according to the Kattan's nomogram predicted progression free probability, laparoscopic radical prostatectomy was effective in controlling cancer at 5 years postoperatively in 53% of men with high risk prostate cancer, confirming the fact that high risk prostate cancer can very well be treated laparoscopically, Hull and colleagues reported a 65% 5-year cancer control in the high risk group defined according to the D'Amico criteria (presence of clinical stage T2c or Gleason sum >7 or PSA greater than 20 ng/ml) and after excluding patients with clinical T3 cancer¹⁵,

while, Kupelian et al. reported a 37% freedom from progression at 5 years after open radical prostatectomy¹⁶. In a risk stratified comparison of oncological outcomes after radical prostatectomy, external beam radiotherapy and brachytherapy with or without hormonal therapy, D'Amico et al. reported lower 5 year freedom from recurrence rates for the high risk patients than our findings or those of Hull et al¹⁷. At our institution the agreed upon definition of biochemical recurrence is 0.1ng/ml confirmed by a subsequent rising PSA level. According to our data, any detectable postoperative PSA should be interpreted as a recurrence of cancer after radical prostatectomy. Other PSA cutoffs have been shown to correlate better with clinically important endpoints such as development of metastases¹⁸.

One particularity about our study is that it includes a consecutive experience starting with the very first patients to undergo laparoscopic radical prostatectomy and most importantly it reflects the evolution of the surgical technique over the last decade as well as the transfer of knowledge from a first to a second generation laparoscopic surgeon. One of such evolutionary process is the change in indications and anatomical limits of pelvic lymph node dissection during laparoscopic radical prostatectomy. By extending the template of PLND to include the external iliac, hypogastric and obturator fossa nodal groups, detection of nodal metastases significantly increased by a threefold. While this finding is not new and has clearly been demonstrated by Bader and coll¹⁹, it does confirm that an extended PLND is feasible laparoscopically and any lesser anatomical variant is inadequate to properly detect nodal metastasis²⁰.

CONCLUSION

Laparoscopic radical prostatectomy provided 5 and 8-year biochemical recurrence free survival in 79% and 71% of patients with clinically localized prostate cancer, and 53% at 5-years of those with high risk cancers. A pelvic lymph node dissection limited to the external iliac nodal group is inadequate for detecting nodal metastases.

These data establish the maturity of the laparoscopic technique and could be used as a proof of principle in designing clinical trials comparing the oncological efficacy of laparoscopy to other treatment modalities in men with low, intermediate or high risk prostate cancers.

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Figure 1.
Kaplan-Meier probability of freedom from progression, with 95% confidence intervals

Figure 2.
Kaplan-Meier probability of freedom from progression by preoperative risk.

Figure 3.
Kaplan-Meier freedom from Progression by surgical margin status

Figure 4.
Kaplan-Meier by pathologic risk group

Table 1

Clinical and pathologic characteristics. Data are given as median (interquartile range) or frequency (%)

Age at RP (years) (n=1419)	61 (56, 66)
Preoperative PSA (ng/ml) (n=1415)	6.08 (4.28, 8.75)
Preoperative nomogram probability of recurrence at 5 years (%) (n=1231)	13 (9, 20)
Low risk (0–10%)	443 (36%)
intermediate risk (10–30%)	642 (52%)
High risk (30–100%)	146 (12%)
Clinical stage (n=1392)	
T1	967 (69%)
T2a	150 (11%)
>T2a	275 (20%)
Biopsy Gleason grade (n=1363)	
<7	886 (65%)
7	405 (30%)
>7	72 (5%)
Pathologic Gleason grade (n=1383)	
<7	501 (36%)
7	794 (57%)
>7	88 (6%)
Extracapsular extension (n=1331)	357 (27%)
Seminal vesicle invasion (n=1384)	75 (5%)
Non-organ confined disease (n=1314) *	378 (29%)
Positive surgical margins (n=1384)	173 (13%)

* Presence of ECE, SVI, or LNI

Table 2

Summary of lymph node dissection and lymph node involvement

	Overall (n=1422)	Before 2/1/2005 (n=849)	After 2/1/2005 (n=573)
Lymph node dissection performed	828 (58%)	262 (31%)	566 (99%)
Number with predicted probability of lymph node involvement>1%	962	596	366
Lymph node dissection performed	603 (63%)	239 (40%)	364 (99%)
Lymph node involvement	45 (7%)	7 (3%)	38 (10%)
Median number of nodes removed (range)	12 (1, 48)	9 (1, 27)	13 (2, 48)